# Guide B

# Vaccination Guidelines for State and Local Health Agencies

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**The State Epidemiologist, health officer, or other authorized health or state official should assign a person or persons to assume organizational responsibilities for state and local resources for vaccine administration during a smallpox outbreak. This person(s) should work with federal and other state emergency management authorities to implement the following vaccine administration strategies.**

### 1. Overall Vaccination Strategy

**Background -** Throughout the smallpox eradication program, vaccination of close contacts to smallpox cases played the most important role in stopping transmission of disease. When large numbers of cases occurred, public health authorities sometimes supplemented this strategy with broader vaccination campaigns to increase the level of community immunity to smallpox. However, targeted vaccination of close contacts is the mainstay of smallpox outbreak control as it assures the administration of vaccine to those with the greatest risk of developing smallpox (and thus the greatest need for vaccination) and limits the number of unnecessary vaccinations in those individuals with little risk of disease (least need for vaccination). In addition, although smallpox vaccine is safe and effective, vaccine adverse events can occur in a small number of vaccine recipients, especially those with immune system deficiencies. Therefore, vaccinating individuals based on their risk of developing disease will help minimize adverse events in those who have a low risk of contracting smallpox but a high risk of adverse reactions to the vaccine.

Once a smallpox outbreak has been confirmed, public health officials must implement the following rapid outbreak containment measures:

1. enhanced surveillance to quickly identify other potential cases (see Guide A)
2. appropriate isolation of potential cases during their evaluation to prevent further transmission (see Guide C)
3. identification of contacts to potential cases (see Guide A)
4. vaccination and monitoring of contacts and their household contacts
5. vaccination of noncontact high-risk personnel

The following activities must also take place to support vaccination administration in a smallpox emergency:

1. Establish controlled, non-hospital vaccination sites for contacts or other broader public vaccination campaigns that may be implemented.
    a. Must have appropriate vaccine storage capabilities (vaccine stored at 2 to 8 °C).
    b. Must have space to allow for personnel to provide screening, vaccination, and education of vaccine recipients.
    c. Must have communication capabilities including at least telephone and fax capabilities.

d. Must have adequate security to provide safe storage of vaccine and protection for personnel.
e. Must have equipment needed for resterilization of needles, if required.

2. Establish controlled, nonhospital vaccination sites for medical, public health, or other designated responders.
   See (a-d) above
3. Establish a system for vaccine adverse events tracking and reporting.

Detailed information on conducting smallpox vaccination clinics in found in Annex 2 and Annex 3 of this document.

## Vaccination Strategies for Control

**Primary Strategy: Contact Identification and Vaccination** - Contact vaccination is based on identifying a case of smallpox and vaccinating the persons who have or are most likely to come into contact with the smallpox case as these are the people that have the greatest chance of developing the disease. If contacts can be vaccinated within 4 days of their contact with the smallpox case, they may be protected from developing the disease or may at least develop a less severe illness. Since smallpox is usually transmitted by close contact except under special circumstances (to be discussed later in this section), people with face-to-face or household contact with a smallpox case are the ones at greatest risk for developing the disease and should be prioritized for vaccination.

Individuals most likely to come into contact with an asymptomatic (not exhibiting signs or symptoms of smallpox) contact to a smallpox case (i.e., household members of a contact) should also be vaccinated to prevent infection of those individuals, should the initial smallpox contact later develop the disease. In addition, contagious individuals (those with a rash) must be isolated to prevent contact with nonvaccinated or susceptible individuals during their period of infectiousness (from onset of rash until all scabs have fallen off), further limiting the opportunity for disease transmission. Intensive surveillance for other contacts and potential cases in the area will help to quickly identify other groups for focal vaccination and isolation.

Smallpox vaccination strategies in an outbreak will be based on:

1. Quickly identifying and isolating smallpox cases.
2. Identifying and vaccinating their close contacts.
3. Monitoring the vaccinated contact and isolating the contact if fever develops.
4. Vaccinating household members of contacts without contraindications to protect them if the contact develops smallpox. Household members of contacts who cannot be vaccinated because of contraindications should avoid contact with the contact until the incubation period for the disease has passed (18 days) or 14 days following successful vaccination of the contact.
5. Vaccinating health-care and public health workers (physicians, nurses, EMTs, etc.) who will be directly involved in evaluating, treating, transporting, or interviewing potential smallpox cases.

6. Vaccinating other response personnel who have a reasonable probability of contact with smallpox patients or infectious materials (e.g., selected law enforcement, emergency response, or military personnel).

Procedures for vaccination follow-up to confirm vaccine take will utilize a vaccine site reaction recognition card given to vaccine recipients at the time of vaccination. If personnel resources permit, vaccine takes should be confirmed and recorded by health personnel 7 days following vaccination. If personnel resources do not permit direct follow-up for vaccine take confirmation, recipients will have instructions to call for evaluation if the vaccine site does not look similar to that depicted on the card at day 7.

**Supplemental Strategy -** A broader vaccination campaign to increase community immunity to smallpox may be instituted by federal public health authorities in addition to continuing contact tracing and vaccination activities under the following conditions:

1. The initial number of smallpox cases or identified locations of smallpox outbreaks is considered too large to allow contact tracing with vaccination to be effective as the only vaccination strategy for outbreak containment.
2. New cases fail to show a decline after two or more generations from the initially identified case(s)

Initial outbreak control measures fail to show a decline in the number of new cases after approximately 30% of the current stores of vaccine have been utilized.

Use of Diluted Vaccine

Because of the supplies of smallpox vaccine are currently limited, it may be necessary to utilize diluted preparations of the vaccine to support any broader vaccination campaigns that may be instituted as a supplemental strategy for outbreak control. In addition, diluted preparations of vaccine may be utilized to vaccinate response personnel who require vaccination for anticipated exposures but who otherwise have an appropriate amount of time to assure a vaccine take before they begin activities that may expose them to smallpox virus. Decisions regarding, 1) the institution of vaccination utilizing diluted vaccine, 2) the dilution that will be utilized, and 3) the persons for which diluted vaccine is indicated, will be determined by Federal public health authorities based upon continuing assessments of the outbreak progression and vaccine availability. Once the decision to utilize diluted vaccine has been made, protocols for preparing and initiating vaccination with diluted vaccine will be distributed to state and local public health authorities. As additional supplies of the vaccine becomes available these recommendations may be subject to change and readers should consult the CDC website at www.cdc.gov/smallpox for updates.

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| Vaccination to include groups other than those listed below or use of diluted vaccine should not be implemented unless initiated by federal public health authorities (Director of the CDC or Secretary of HHS). |

## 2. Indications for Vaccination During a Smallpox Emergency

By far, the most common mode of transmission of smallpox from person to person is from spread through direct deposit of infective droplets onto the nasal or oral mucosal membranes, or into the alveoli of the lungs of a susceptible person. This generally requires close face-to-face contact (≤6.5 feet) as the droplets do not travel more than a few feet in the air before settling out onto the ground. Much less commonly and under certain circumstances, smallpox can be spread by fine-particle aerosols that can travel in the air greater distances than droplets. This type of spread usually occurred in hospital settings where more severe cases of smallpox or cases with a cough were admitted and not isolated to areas of the hospital that had air supply and ventilation systems separate from other areas. Even less commonly, smallpox can be spread by contact with contaminated materials.

In a smallpox outbreak, the following high-risk groups will be prioritized for vaccination:

1) Persons who were exposed to the initial release of the virus.

2) Persons who had face-to-face, household, or close-proximity contact (≤ 2 meters = 6.5 feet) with a confirmed or suspected smallpox patient after the patient developed fever and until all scabs have separated (no longer infectious).

3) Personnel selected for the direct medical or public health evaluation, care, or transportation of confirmed, probable, or suspected smallpox patients.

4) Laboratory personnel selected for the collection or processing of clinical specimens from confirmed, probable, or suspected smallpox cases.

5) Other persons with increased likelihood of contact with infectious materials from a smallpox patient such as laundry or medical waste handlers for a facility where smallpox patients are admitted.

6) Other groups whose unhindered function is deemed essential to the support of response activities and who are not otherwise involved in patient-care activities but who have a reasonable probability of contact with smallpox patients or infectious materials (e.g., selected law enforcement, emergency response, or military personnel).

7) Because of the potential for greater spread of smallpox in a hospital setting due to aerosolization of the virus from a severely ill patient, consideration should be given to vaccination of all individuals present in the hospital during the time a case was present and not isolated in an appropriate manner in a

room with ventilation separate from other areas of the hospital (see Isolation Guidelines).

Because smallpox is transmitted only by those who are obviously sick with a rash, categories of otherwise essential personnel (e.g., firemen, police, and municipal officials) who are not involved in activities that have a reasonable probability of contact with smallpox patients or infectious materials do not require priority vaccination.

## 3. Contraindications for Vaccination of Noncontacts During a Smallpox Emergency

**In general, the risk of developing smallpox for face-to-face contacts with smallpox cases outweighs the risk of developing complications for those smallpox case contacts with contraindications.**

**Household members of contacts with contraindications to vaccination should consider housing themselves separately from vaccinated household members until the vaccination site has healed to decrease the risk of contact transmission of virus.**

Persons with certain medical conditions are known to have a higher risk of developing severe complications following vaccination with vaccinia vaccine (smallpox vaccine). These include:

1. Persons with diseases or conditions which cause immunodeficiency, such as HIV, AIDS, leukemia, lymphoma, generalized malignancy, agammaglobulinemia, or therapy with alkylating agents, antimetabolites, radiation, or large doses of corticosteroids.

   *A household member who has an immunodeficiency disease or is undergoing one of the therapies listed who is exposed to a recently vaccinated household member is also at risk of developing a postvaccine complication from potential accidental inoculation with virus from the vaccination site of the vaccinated person.*

2. Persons with serious, life-threatening allergies to the antibiotics polymyxin B, streptomycin, tetracycline, or neomycin.

3. Persons who have ever been diagnosed with eczema, even if the condition is mild or not presently active.

   *A household member who has eczema or a history of eczema who is exposed to a recently vaccinated household member, is also at higher risk for developing a postvaccine complication from potential accidental inoculation with virus from the vaccination site of the vaccinated person.*

4. Women who are pregnant.

5. Persons with other acute or chronic skin conditions such as atopic dermatitis, burns, impetigo, or varicella zoster (shingles) should not be vaccinated until the condition resolves.

In general, individuals with the above conditions should not be vaccinated unless they have been exposed to smallpox virus. Where there is uncertainty as to the level of exposure to the virus, the risks verses benefits of vaccination must be evaluated.

## 4. Reconstitution, Administration, and Storage of Vaccinia Vaccine

**The current vaccine is no longer licensed because of required changes in the diluent preparation for vaccine reconstitution. These changes in diluent do not affect the ability of the vaccine to produce immunity to smallpox. However, because the vaccine is no longer licensed, it must be labeled as an Investigational New Drug (IND).**

Dryvax® smallpox vaccine was manufactured as a lyophilized preparation of live vaccinia virus. The vaccine was prepared from calf lymph with a seed virus derived from the New York City Board of Health (NYCBOH) strain of vaccinia. The calf lymph is purified, concentrated, and dried by lyophilization. The reconstituted vaccine contains approximately 100-million living vaccinia viruses (approximately $10^8$ PFU) per mL. It is a highly effective immunizing agent that brought about the global eradication of smallpox. Recent testing has shown that the current vaccine has retained adequate potency during the extended storage period since its production.

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**Reconstitution of Vaccine with Commercially Packaged Diluent**

Diluent is required for the reconstitution of the smallpox vaccine prior to administration. The previously licensed diluent for use with smallpox vaccine contained 50% glycerin, 0.25% phenol in Sterile Water for Injection, USP, and 0.005% brilliant green. Reconstitution of a single vial of smallpox vaccine with 0.25 mL of diluent would yield approximately 100 doses. However, this pre-packaged diluent is no longer available. The diluent that will be used in this protocol is similar in formulation to the licensed diluent except that it lacks the 0.005% brilliant green. This change in formulation does not affect **the ability of the vaccine to produce immunity to smallpox**

Directions for Reconstitution

1. Remove vaccine vial from refrigerated storage and allow vial to come to room temperature.

2. Lift up tab of aluminum seal on vaccine vial. DO NOT BREAK OFF OR TEAR DOWN TAB.

3. Wipe off vial stopper with an alcohol pad and allow it to dry.

4. Place vaccine vial upright on a hard, flat surface.

5. Remove cap from the prefilled syringe. Take a 1.0-cc syringe (e.g., tuberculin syringe) and withdraw 0.25 mL from the opening in the prefilled diluent syringe. Inject the 0.25 mL of the diluent in the 1.0-cc syringe into the vaccine vial to reconstitute the vaccine.

6. Withdraw needle and syringe and discard in the appropriate biohazard sharps container.

7. Allow the vaccine vial to stand undisturbed for 3 to 5 minutes. Then, if necessary, swirl vial gently to effect complete reconstitution.

8. In the space provided on the vaccine vial label, record the date and time that the diluent vial was entered for the purpose of vaccine reconstitution. The vaccine is now ready for use.

9. **Reconstituted vaccine may be used for 3 months if stored at 2 to 8 ºC when not in actual use.**

NOTE: The vaccine vial, its stopper, the diluent syringe, the needle used for diluent reconstitution of the vaccine, and any gauze or cotton that came in contact with the vaccine should be burned, boiled, or autoclaved before final disposal (see Guide F – Decontamination Guidelines).

Administration of Reconstituted Vaccine

1. Gloves should be worn when handling opened vaccine vials, used bifurcated needles, administering vaccine, or evaluating a vaccination site. Care should be taken to prevent bacterial contamination of the opened vaccine vial or vaccination site, or self-inoculation of virus to other sites (see Recognition of Adverse Events, below).

2. Remove aluminum seal from vaccine vial by pulling down “tear off” tab.

3. Remove rubber stopper from vaccine vial and place in sterile container (stopper will be used to recap vials containing vaccine).

4. The site of vaccination should be one that is easily accessible for vaccination and evaluation of vaccine take on postvaccination day 7. The outer aspect of the upper right arm over the insertion of the deltoid muscle should be used as the standard vaccination site in order to prevent confusion with the vaccination site from a previous vaccination.

5. Cleaning the vaccination site is not necessary unless grossly contaminated. If cleaning is deemed necessary, clean the site with alcohol and let dry thoroughly. It is essential the site be allowed to dry thoroughly in order to avoid inactivation of the vaccine deposited on the skin.

6. Dip the bifurcated point of a sterile bifurcated needle into the vial of reconstituted vaccine and withdraw the needle perpendicular to the floor.

7. Do not redip the needle into the vaccine vial if the needle has touched the skin.

8. Holding the skin of the upper arm taut, the vaccinator should place his/her wrist firmly on the arm. Holding the needle at a 90° angle (perpendicular) to the skin, apply **15** up-and-down (perpendicular) strokes rapidly within a 5mm diameter area [Fig. 3]. The strokes should be made rapidly, and be sufficiently vigorous to illicit a trace of blood at the vaccination site. If a trace of blood does not appear, the strokes have not been sufficiently vigorous and the procedure should be repeated.

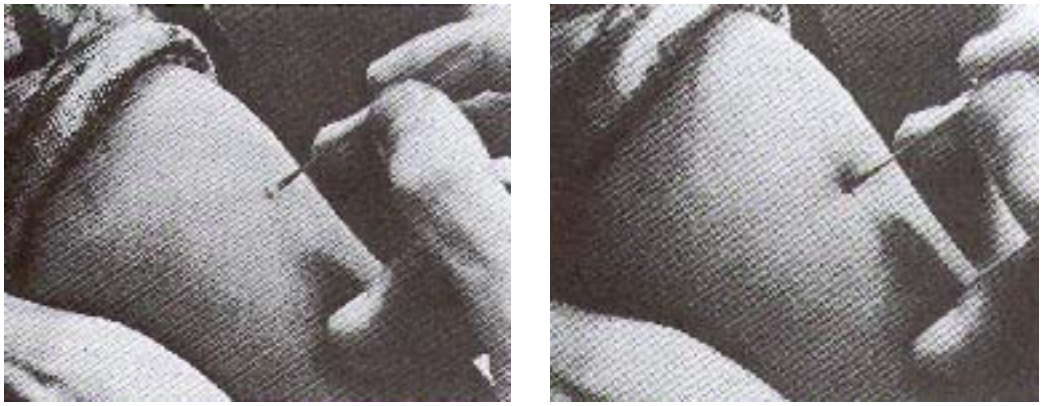

Fig. 3 – Needle held at a 90° angle to skin then rapid, up-and-down perpendicular strokes are used to administer the vaccine. [Fenner F, Henderson, DA, et al. Smallpox and its eradication. WHO. 1988, Reprinted with permission of WHO]

9. Vaccinia virus may be recovered from the site of vaccination beginning at the time of development of a papule (2 to 5 days postvaccination) until the scab separates from the skin (14 to 21 days postvaccination). The vaccination site can

be covered with a porous bandage such as gauze until the scab has separated and the underlying skin has healed, in order to prevent contact transmission of the virus to unvaccinated persons (people with contraindications to vaccination) or inadvertent inoculation of another body site (see Adverse Events below). The site should be kept dry, however normal bathing can occur.

10. Dispose of the bifurcated needle in a medical waste sharps container or re-sterilize per directions given below for sterilization and re-use of bifurcated needles.

11. If vaccine is to be stored for subsequent use, recap vial with the sterile rubber stopper and store capped vial at 2 to 8 ºC.

Note: If unsterilized needles are being used or if needles are in short supply and you have to clean and resterilize, please see CDC Recommendations for Handling, Cleaning and Sterilizing Bifurcated Immunization Needles in Healthcare Settings before beginning vaccination procedures (Section H).

## 5. Recognition of Expected Vaccine Reactions/Take

Successful vaccination, is normally associated with tenderness, redness, swelling, and a lesion at the vaccination site. Primary vaccination may also be associated with fever for a few days and enlarged, tender lymph nodes in the axilla of the vaccinated arm. These symptoms are more common in persons receiving their first dose of vaccine (15 to 20%) than in persons being revaccinated (0 to 10%).

A primary (major) reaction results from successful primary vaccination of a non-vaccinated individual. It is expected that the majority of individuals will exhibit this type of reaction as most have never received vaccination or were vaccinated over 20 years ago. Reactions other than a primary or major reaction in an individual receiving their first-ever vaccination or revaccination after many years should be interpreted as an unsuccessful vaccination, and the individual should be revaccinated.

1. Primary (major) reaction – The inoculation site becomes reddened and pruritic 3-4 days after vaccination. A vesicle surrounded by a red areola then forms which becomes umbilicated and then pustular by the 7$^{th}$ to 11$^{th}$ day after vaccination. The red areola has enlarged by this time. The pustule begins to dry, the redness subsides, and the lesion becomes crusted between the 2$^{nd}$ and 3$^{rd}$ week. (Fig. 4) By the end of the 3$^{rd}$ week, the scab falls off leaving a permanent scar that at first is pink in color but eventually becomes flesh-colored.

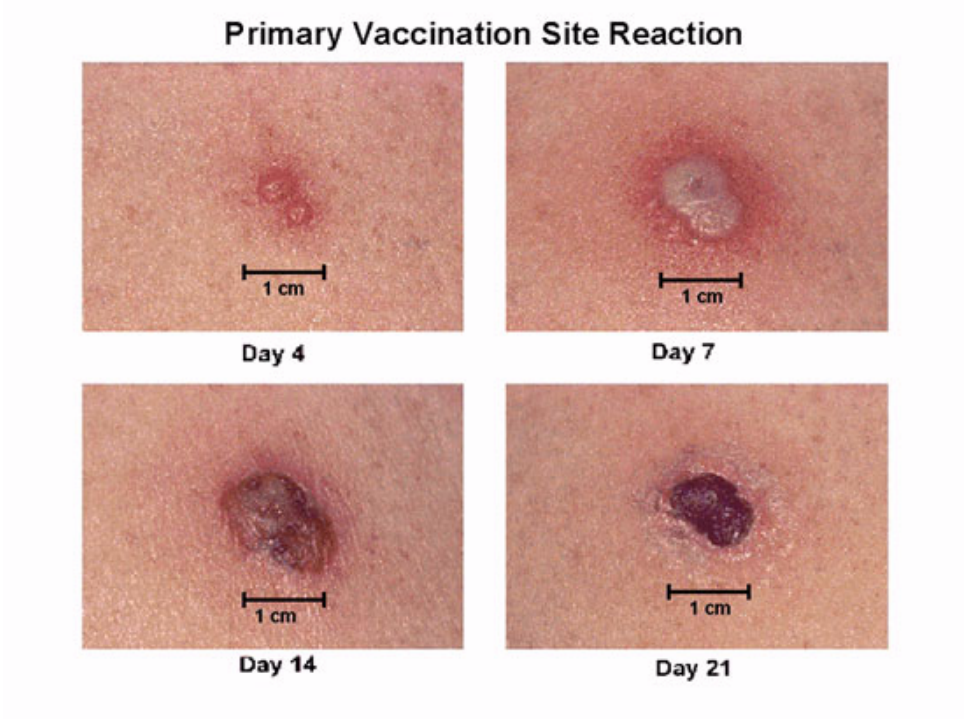


Fig. 4 - Major (primary) reaction: Expected vaccine site reaction and progression following primary smallpox vaccination or revaccination after a prolonged period between vaccinations. Multiple pressure vaccination technique used. Source: CDC.

At the end of the first week between the vesicular and pustular phases, there may be a variable amount of fever, malaise, and regional lymphadenitis. These symptoms usually subside within 1 to 2 days and are more likely to occur in older children and adults than in infants.

Revaccination of a person who has been vaccinated within the last 10 years (a partially immune person) is usually followed by an attenuated primary vaccine site reaction with the following characteristics: 1) absence of fever or constitutional symptoms, 2) papule by 3$^{rd}$ day that becomes vesicular by 5 to 7$^{th}$ day, and dries shortly thereafter, 3) a relatively small vesicle and areola, and 4) the scar, if present, is usually insignificant and disappears within 1 to 2 years.

2. A delayed type of skin sensitivity consisting of erythema only within 24 to 48 hours may occur following killed as well as live vaccine. Under these circumstances, it represents a response to inert protein in a previously sensitized person. This type of reaction can occur in a highly immunized person or in individuals with little or no immunity and is indistinguishable from the immediate or immune reaction. Therefore, persons exhibiting this type of reaction should be revaccinated (Fig. 5).

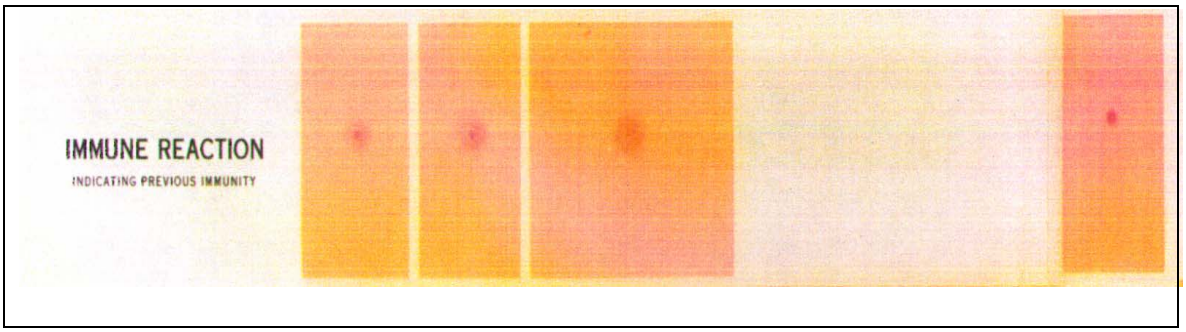


Fig. 5 – Attenuated reaction in an immune person that can also represent a response to an inert protein without development of immunity. Individuals with this reaction should be revaccinated.

**Confirmation of Successful Vaccination**

Successful take of vaccination should be contingent upon the presence of a pustular lesion in a previously unvaccinated persons and a pustular lesion or an area of definite induration or congestion surrounding a central lesion, 7 days following revaccination in a previously vaccinated person. Vaccinees who do not exhibit the type of "major" reaction at the vaccination site on day 7 illustrated in Figure 4 should be revaccinated.

## 6. Recognition of Adverse Reactions (AEs)

The overall risk of serious complications following vaccination with vaccinia vaccine is low. Complications occur more frequently in persons receiving their first dose of vaccine, and among young children (≤5 years of age). The most frequent complications of vaccination and their descriptions are listed below:

G. *Inadvertent inoculation at other sites* – This is the most frequent complication of vaccinia vaccination and accounts for about 50% of all complications following primary and revaccination. This complication occurs at a rate of about 1 in 2000 primary vaccinations and usually results from auto-inoculation when the virus is transferred by hand from the site of vaccination to other areas. The most common sites involved are the face, eyelid (Fig. 6), nose, mouth, genitalia, and rectum. Most lesions will heal without specific therapy, but Vaccinia Immune Globulin (VIG) may be useful for some cases of inadvertent ocular inoculation (see Indications and Guidelines for VIG Use below). Inadvertent inoculation can be prevented by handwashing after touching the vaccination site.